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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/844,653	04/27/2001	Julia E. Richards	UM-06105	1588

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EXAMINER	
SOUAYA, JEHANNE E	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 05/06/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/844,653	RICHARDS ET AL.	
	Examiner	Art Unit	
	Jehanne E Souaya	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24-26* is/are rejected.

7)☒ Claim(s) *27* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Newly added claims 24-27 are pending in the instant application. The subject matter of claims 24-26 was indicated as being enabled in the previous office action. However, upon further review, issues regarding enablement of claims 24-26 are set forth below under 35 USC 112, first paragraph. Accordingly, this action is made NON-FINAL.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Objections

3. Claim 27 is objected to because of the following informalities: The claim lacks a modifier or article before the recitation of "nucleic acid sequence". Further, the claim is dependent on a rejected claim. Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. Claims 24-26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid comprising SEQ ID NO 1 or the complement of SEQ ID NO 1, does not reasonably provide enablement for an isolated nucleic acid sequence encoding a polypeptide of SEQ ID NO 3, or vectors or host cells comprising such. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The claims are drawn to a composition comprising an isolated nucleic acid sequence that encodes SEQ ID NO 3, and vectors and host cells comprising such nucleic acids. The specification does not enable the skilled artisan to use nucleic acid sequences that encode SEQ ID NO 3 because the specification does not enable the skilled artisan to use the polypeptide of SEQ ID NO 3, without further unpredictable and undue experimentation. The specification teaches that a splice variant of SEQ ID NO 1 was mapped to a previously known glaucoma inclusion interval on chromosome 4. Although nucleic acids to the full length of SEQ ID NO 1 could be used to map a disease locus, claim 24 encompasses a large genus of degenerate variants of SEQ ID NO 1 that could not be used to make specific probes.

The specification teaches that SEQ ID NO 1 encodes human latrophilin 3, LPH3(SEQ ID NO 3). The specification teaches that SEQ ID NO 3 is a member of the latrophilin family (p. 4), which are G protein coupled receptors. Identifying a protein as a G protein coupled receptor, however, does not provide a skilled artisan with a predictable determination as to the function of the receptor because G protein coupled receptors are a diverse group of receptors which bind structurally and functionally different ligands. For example, Ji et al (The Journal of Biological Chemistry, vol. 28, 1998, pp 17299-17302) teach that nearly 2000 G protein coupled receptors are known and that such have been classified into over 100 subfamilies based on homology, ligand structure, and receptor function. The only function or biological activity asserted for the polypeptide of SEQ ID NO 3 by the specification is binding of the TIGR peptide (p. 4), however the specification has not demonstrated such (mutations in TIGR are associated with primary open angle glaucoma). The specification contemplates that LPH3 is the TIGR receptor and that binding occurs through each protein's olfactomedin domain (see p. 52), however neither the art

nor the specification provide support that receptors and ligands bind via olfactomedin domains such that the skilled artisan could predictably conclude that because LPH3 contains an olfactomedin domain, it will bind TIGR via such. The specification teaches that variants of the protein of SEQ ID NO 3 could be used in assays to determine increased susceptibility to eye disease (p. 52). While the specification teaches a number of amino acid variants for LPH3 (see example 3, pp 88-91), none of these variants have been associated with either eye disease, glaucoma, or aberrant activity of LPH3. The specification does not teach how these amino acid changes affect the activity of LPH3, whereas such teaching is critical for the skilled artisan to be able to determine the function of LPH3 or to establish a predictable correlation between variants of LPH3 and eye disease in general, or glaucoma specifically. The art does not make up for the deficiencies in the specification has the art does not teach a specific function for the LPH3 polypeptide.

The specification teaches that mRNA encoding LPH3 was found to be expressed in trabecular meshwork cells, which are the cells that express the TIGR protein. The specification then concludes, that LPH3 is therefore the TIGR receptor. However, without demonstrating such, the specification has not enabled the skilled artisan to predictably conclude that LPH3 is the TIGR receptor based on the observation the mRNA encoding LPH3 is expressed in the same cells as TIGR because trabecular meshwork cells would be expected to express a large number of different mRNAs, whereas all of these mRNAs would not be expected to encode proteins that will bind TIGR peptide. It is noted that experimentation is being conducted to determine whether LPH1, a homolog of LPH3, is the TIGR receptor.

From: www.glaucoma.org/research/fund_pilot.html

Julia Richards, PhD & Frank Rozsa, PhD,
University of Michigan, Ann Arbor, MI:
"Identification and Characterization of a Trabecular Meshwork Inducible Glucocorticoid Response (TIGR)-Binding Protein on the Trabecular Meshwork Cell Surface."

Identified latrophilin (LPH1) as a potential TIGR binding protein based on its structure and properties. Observed that LPH1 is co-expressed with TIGR in trabecular meshwork cells. Tested hypothesis that the latrophilin (LPH1) protein is a TIGR protein receptor.

Significance: By confirming the LPH1 as a TIGR protein receptor, it can be determined if LPH1 causes primary open-angle glaucoma in conjunction with the TIGR protein and/or by itself.

The basis for this hypothesis appears to be the same as that taught in the specification, that LPH1 was observed to be co-expressed with TIGR in trabecular meshwork cells. However, Matsushita et al teach that while LPH3 and LPH1 are homologous, proteins in this family are heterogeneous with distinct tissue distribution and functions and are likely to interact with different ligands (FEBS Letters, vol. 443, pp 348-52; see abstract, and p. 352, col. 1, last para).

Therefore, based on the lack of guidance in the specification and the teachings in the art, the skilled artisan would not be able to predictably conclude a function for the LPH3 polypeptide without empirical research which would include a large amount of trial and error analysis. To determine a use for the polypeptide of SEQ ID NO 3, the skilled artisan would be required, for example, to confirm that LPH3 is a TIGR receptor, however such analysis is unpredictable based on the lack of guidance in the specification and the teaching of unpredictability taught in the art with regard to latrophilin function, and is considered undue. Alternatively, the skilled artisan would be required to determine the biological activity or function of the polypeptide of SEQ ID NO 3, for example to identify it's ligand, the signal transduced, etc, or to determine whether aberrant expression or function of SEQ ID NO 3 was associated with a specific disease (which neither the specification nor the art teach). Such experimentation would require a large amount of trial and error analysis, the results of which are unpredictable, and is considered undue.

Conclusion

5. No claims are allowable. Claim 27 is objected to for being dependent on a rejected claim.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Souaya whose telephone number is (703) 308-6565. The examiner can normally be reached Monday-Friday from 9:00 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 305-3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Jehanne Souaya
Patent examiner
Art Unit 1634

Jehanne Souaya
5/2/2003